

AMENDMENTS TO THE CLAIMS

This Listing of Claims will replace all prior versions, including listings, of claims in the application.

Listing of Claims

Claim 1 (original): An isolated peptide selected from the group consisting of:

- (a) a peptide set forth in Tables 1-14; and
- (b) a derivative of the peptide in (a).

Claim 2 (original): The isolated peptide of claim 1, wherein Xaa1 is Glu or γ -carboxy-Glu, Xaa2 is Gln or pyro-Glu, Xaa3 is Pro or hydroxy-Pro, Xaa4 is Trp or bromo-Trp, and Xaa5 is Tyr, 125 I-Tyr, mono-iodo-Tyr, di-iodo-Tyr, O-sulpho-Tyr or O-phospho-Tyr.

Claim 3 (original): The derivative of the peptide of claim 1, in which the Arg residues may be substituted by Lys, ornithine, homoarginine, nor-Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any synthetic basic amino acid; the Lys residues may be substituted by Arg, ornithine, homoarginine, nor-Lys, or any synthetic basic amino acid; the Tyr residues may be substituted with meta-Tyr, ortho-Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any synthetic hydroxy containing amino acid; the Ser residues may be substituted with Thr or any synthetic hydroxylated amino acid; the Thr residues may be substituted with Ser or any synthetic hydroxylated amino acid; the Phe residues may be substituted with any synthetic aromatic amino acid; the Trp residues may be substituted with Trp (D), neo-Trp, halo-Trp (D or L) or any aromatic synthetic amino acid; the Asn, Ser, Thr or Hyp residues may be glycosylated; the Tyr residues may also be substituted with the 3-hydroxyl or 2-hydroxyl isomers

(meta-Tyr or ortho-Tyr, respectively) and corresponding O-sulpho- and O-phospho-derivatives; the acidic amino acid residues may be substituted with any synthetic acidic amino acid, e.g., tetrazolyl derivatives of Gly and Ala; the aliphatic amino acids may be substituted by synthetic derivatives bearing non-natural aliphatic branched or linear side chains C_nH_{2n+2} up to and including n=8; the Leu residues may be substituted with Leu (D); the Glu residues may be substituted with Gla; the Gla residues may be substituted with Glu; the N-terminal Gln residues may be substituted with pyroGlu; the Met residues may be substituted by Nle; the Cys residues may be in D or L configuration and may optionally be substituted with homocysteine (D or L); and pairs of Cys residues may be replaced pairwise with isoteric lactam or ester-thioether replacements, such as Ser/(Glu or Asp), Lys/(Glu or Asp), Cys/(Glu or Asp) or Cys/Ala combinations.

Claim 4 (withdrawn): An isolated nucleic acid encoding an conotoxin propeptide having an amino acid sequence set forth in Table 1.

Claim 5 (withdrawn): The isolated nucleic acid of claim 4, wherein the nucleic acid comprises a nucleotide sequence set forth in Table 1.

Claim 6 (original): An isolated conotoxin propeptide having an amino acid sequence set forth in Table 1.

Claim 7 (withdrawn): A method of alleviating pain in an individual which comprises administering to said individual that is either exhibiting pain or is about to be subjected to a pain-causing event a pain-alleviating amount of an active agent comprising a pain-relieving conotoxin peptide of claim 1 or a pharmaceutically acceptable salt thereof.

Application No.: 10/072,602
Supplemental Amendment Dated 20 July 2004
Further reply to Office Action of 9 June 2004

Claim 8 (withdrawn): A method for treating or preventing disorders associated with a disorder selected from the group consisting of voltage-gated ion channel disorders, ligand-gated ion channel disorders and receptor disorders in an individual which comprises administering to an individual in need thereof a therapeutically effective amount of a conotoxin peptide of claim 1 or a pharmaceutically acceptable salt thereof.

Claim 9 (withdrawn): A method of identifying compounds that mimic the therapeutic activity of a conotoxin, comprising the steps of: (a) conducting a biological assay on a test compound to determine the therapeutic activity; and (b) comparing the results obtained from the biological assay of the test compound to the results obtained from the biological assay of a conotoxin.

Claim 10 (Currently amended): An isolated A substantially pure conotoxin peptide derivative comprising a permutant of the peptide of claim 1.

Claim 11 (Currently amended): An isolated A substantially pure conotoxin peptide derivative comprising a permutant of the peptide of claim 2.

Claim 12 (withdrawn): Use of a radiolabeled conotoxin peptide of claim 1 for characterization of a new site on the aforementioned receptors or channels and use of these peptide probes for screening and identification of novel small molecules that interact at the aforementioned sites.

Claim 13 (withdrawn): The use of claim 12, wherein said receptor or channel is a monoamine transporter.

Application No.: 10/072,602
Supplemental Amendment Dated 20 July 2004
Further reply to Office Action of 9 June 2004

Claim 14 (withdrawn): The use of claim 13, wherein said peptide is selected from the group of peptides set forth in Table 5.

Claim 15 (Currently amended): The isolated peptide of claim 1 selected from the group consisting of:

ZTCCGYRMCVPC (SEQ ID NO:523);
~~ACCGYKLCSPC (SEQ ID NO:524);~~
~~STCCGFKMCIPCR (SEQ ID NO:525);~~
STCCGFKMCIPCS (SEQ ID NO:526);
STCCGFKMCIPC (SEQ ID NO:527);
STCCGYRMCVPC (SEQ ID NO:528);
NGVCCGYKLCLPC (SEQ ID NO:529);
LCCGFWMCIPCN (SEQ ID NO:530);
~~NGVCCGYKLCHOE (SEQ ID NO:531);~~
~~EVCCGYKLCHOE (SEQ ID NO:532);~~
SVCCGYKLCFPC (SEQ ID NO:534);
NGVCCGYRMCVPC (SEQ ID NO:535);
ZACCGFKMCVPC (SEQ ID NO:537);
NGVCCGFWMCIPCN (SEQ ID NO:539);
DVCCYVRMCP.CR (SEQ ID NO:540); and
derivatives thereof.

Claim 16 (previously presented): The isolated peptide of claim 15 selected from the group of:

SVCCGYKLCFPC (SEQ ID NO:534) and
derivatives thereof.

Application No.: 10/072,602
Supplemental Amendment Dated 20 July 2004
Further reply to Office Action of 9 June 2004

Claim 17 (previously presented): The isolated peptide of claim 16 that is SVCCGYKLCFPC (SEQ ID NO:534) .

Claim 18 (Currently amended): The isolated conotoxin propeptide of claim 6 selected from the group of conotoxin propeptides of ~~SEQ ID NO:62, SEQ ID NO:162, SEQ ID NO:229~~, SEQ ID NO:330, SEQ ID NO:333, SEQ ID NO:333, SEQ ID NO:336, SEQ ID NO:339, SEQ ID NO:342, ~~SEQ ID NO:345~~, SEQ ID NO:352, SEQ ID NO:355, SEQ ID NO:361, SEQ ID NO:367 and SEQ ID NO:370.

Claim 19 (previously presented): The isolated conotoxin propeptide of claim 18 that is the conotoxin propeptide of SEQ ID NO:352.

Claim 20 (new). The isolated peptide of claim 15, wherein Pro is substituted by hydroxy-Pro.

Claim 21 (new). The isolated peptide of claim 16, wherein Pro is substituted by hydroxy-Pro.

Claim 22 (new). The isolated peptide of claim 17, wherein Pro is substituted by hydroxy-Pro.

Claim 23 (new): The isolated peptide of claim 1 selected from the group consisting of: Xaa2-Thr-Cys-Cys-Gly-Xaa5-Arg-Met-Cys-Val-Xaa3-Cys-# (SEQ ID NO:230); Asn-Gly-Val-Cys-Cys-Gly-Xaa5-Lys-Leu-Cys-Leu-Xaa3-Cys-^ (SEQ ID NO:331); Ser-Thr-Cys-Cys-Gly-Phe-Lys-Met-Cys-Ile-Xaa3-Cys-Ser-^ (SEQ ID NO:334); Leu-Cys-Cys-Gly-Phe-Xaa4-Met-Cys-Ile-Xaa3-Cys-Asn-^ (SEQ ID NO:337); Ser-Thr-Cys-Cys-Gly-Phe-Lys-Met-Cys-Ile-Xaa3-Cys-# (SEQ ID NO:340); Ser-Thr-Cys-Cys-Gly-Xaa5-Arg-Met-Cys-Val-Xaa3-Cys-# (SEQ ID NO:343); Ser-Val-Cys-Cys-Gly-Xaa5-Lys-Leu-Cys-Phe-Xaa3-Cys-# (SEQ ID NO:353);

Application No.: 10/072,602

Supplemental Amendment Dated 20 July 2004

Further reply to Office Action of 9 June 2004

Asn-Gly-Val-Cys-Cys-Gly-Xaa5-Arg-Met-Cys-Val-Xaa3-Cys-# (SEQ ID NO:356);

Xaa2-Ala-Cys-Cys-Gly-Phe-Lys-Met-Cys-Val-Xaa3-Cys-# (SEQ ID NO:362);

Asn-Gly-Val-Cys-Cys-Gly-Phe-Xaa4-Met-Cys-Ile-Xaa3-Cys-Asn-^ (SEQ ID NO:368); and

Asp-Val-Cys-Cys-Xaa5-Val-Arg-Met-Cys-Xaa3-Cys-Arg-^ (SEQ ID NO:371),

wherein Xaa2 is Gln or pyro-Glu; Xaa3 is Pro or hydroxy-Pro; Xaa4 is Trp (D or L) or bromo-Trp (D or L); Xaa5 is Tyr, ¹²⁵I-Tyr, mono-iodo-Tyr, di-iodo-Tyr, O-sulpho-Tyr or O-phospho-Tyr; ^ is free carboxyl or amidated C-terminus; and # is free carboxyl or amidated C-terminus.

Claim 24 (new). The isolated peptide of claim 23 that is Ser-Val-Cys-Cys-Gly-Xaa5-Lys-Leu-Cys-Phe-Xaa3-Cys-# (SEQ ID NO:353).